

CLAIMS

1. A method of determining whether a substance is an inhibitor or activator of a protein whose production by a cell evokes a responsive change in a phenotypic characteristic other than the level of said protein in said cell per se, which comprises:

(a) providing a first cell line which produces said protein and exhibits said phenotypic response to the protein;

(b) providing a second cell line which produces the protein at a lower level than the first cell line, or does not produce the protein at all, and which exhibits said phenotypic response to the protein to a lesser degree or not at all;

(c) incubating the substance with the first and second cell lines; and

(d) comparing the phenotypic response of the first cell line to the substance with the phenotypic response of the second cell line to the substance.

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2. The method of claim 1 wherein the response is one observable with the naked eye.

3. The method of claim 1 wherein the response is a change in a cultural or morphological characteristic of the cell.

4. The method of claim 1 wherein the response is a change in the ability of the cell line to grow in an anchorage-independent fashion.

51 The method of claim 1 wherein the response is a change in the ability of the cell line to grow on soft agar.

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6. The method of claim 1 wherein the response is a change in foci formation in cell culture.

7. The method of claim 1 wherein the response is a change in the ability of the cells to take up a selected stain.

8. The method of claim 1 in which the protein is an enzyme.

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9. The method of claim 8 wherein increased activity of the enzyme is correlated with increased tumorigenesis.

10. The method of claim 9 in which the enzyme is a protein kinase C enzyme or a fragment, domain or subunit of a receptor which has protein kinase C activity.

11. The method of claim 9 wherein the enzyme is ornithine decarboxylase.

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12. The method of claim 9 in which the protein is the expression product of an oncogene.

13. The method of claim 1 in which the substance is a suspected inhibitor of the biological activity of the protein.

14. The method of claim 1 in which the substance is a suspected activator of the biological activity of the protein.

15. The method of claim 1, wherein said first cell line is obtained by introducing a gene encoding the protein of interest into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

16. The method of claim 15, wherein the gene is introduced into the host cell by means of a first genetic vector into which the gene has been inserted, and said second cell line is obtained by introducing into a similar host cell a second genetic vector essentially identical to the first genetic vector except that it does not bear said gene insert.

17. The method of claim 15 wherein the gene is introduced into the host cell by means of a retroviral vector.

18. The method of claim 15 in which the host cell line essentially does not produce the protein.

19. The method of claim 15 in which the host cell line is a rat-6 fibroblast cell line.

20. The method of claim 3 in which the response is a change in the differentiation state of the cell.

21. A test kit for determining whether a substance is an inhibitor or activator of a protein whose production evokes a responsive change in a phenotypic characteristic other than level of said protein in said cell per se, which comprises:

(a) a first cell line which produces the protein

and exhibits said phenotypic response thereto; and

(B) a second cell line which produces the protein at a lower level than the first cell line, or does not produce the protein, and which exhibits said phenotypic response to the protein to a lesser degree or not at all.

22. The test kit of claim 21, wherein the level of production of the protein in the first cell line is at least five times the level of production of the protein in the second line.

23. The test kit of claim 21, wherein the phenotypic response to expression of the protein is selected from the group consisting of changes in growth rate, saturation density, plating efficiency in soft agar, colony size in soft agar, and combinations thereof.

24. The method of claim 1 wherein the response is a change in an antigenic characteristic of the cell.

25. The test kit of claim 21 wherein said cell lines are mammalian cell lines.

26. The test kit of claim 21, further comprising as a reference reagent a known inhibitor or activator of the protein.

27. The method of claim 15 in which the host cell line is an FDC-P1 cell line.

28. The method of claim 15 in which the host cell line is a CHO cell line.

29. ~~The method of claim 1 in which the protein is an insulin receptor.~~

30. ~~The method of claim 1 in which the protein is a 5 serotonin receptor.~~

INSERT
A1/

add
C2

add 66

see abstract
attached
to Amendment C